A7
CONT.

72. (New) A unit dose formulation according to claim 71 wherein the agent is in admixture with a pharmaceutically acceptable carrier.--

REMARKS

I. Status of Claims

Claims 1-18 and 21-30 are pending in the instant case and stand variously rejected under 35 U.S.C.§112, first and second paragraphs. Claims 31-72 are new. The Applicants acknowledge with thanks the Examiner's rejoinder of Group I with Group III and rejoinder of Group II with Group IV after reconsideration of the original restriction requirement.

Applicants have amended claims 1, 10, 18, 21, 22, and 26-29. Attached hereto is a marked-up version of the changes made to the claims entitled "Version of Markings to Show Changes Made" (Appendix A). For the Examiner's convenience, applicants also have attached on Appendix B entitled "Claims Pending Upon Entry of Instant Amendment" which provides a clean copy of all the claims pending as of entry of the instant amendment.

It will be apparent from the remarks below that most of the amendments made to the pending claims merely adopt the Examiner's suggestions for placing the claims in condition for allowance. The suggestions have been adopted solely to expedite allowance, and not as an acquiescence to any rejection or objection. The amendments are discussed more fully below.

The Applicants have canceled claims 19 and 20 solely because the Patent Office has withdrawn them from consideration, as being directed to a non-elected invention. The Applicants reserve the right to pursue subject matter of any original claim (canceled or amended) in subsequent applications, such as continuing applications. Claim 9 was canceled in view of amendment to claim 1 in which the language the term"... operatively linked to a promoter to promote expression of the VEGF-C in cells of the blood vessel..." was added to claim 1.

The Examiner objected to claims 22-30 because these claims embraced non-elected (in addition to elected) subject matter. The amendments to restrict these claims to the elected invention are made solely to comply with Patent Office

restriction requirement practice and not in response to any rejection or in order to comply with any patentability requirement.

Applicants present new claims 31-72. These claims are fully supported by the specification as filed and the addition of these new claims does not constitute an introduction of new matter into the present application. Support for the new may generally found throughout the specification, in particular, Applicants present herewith Appendix C containing a table which indicates exemplary support in the specification. Briefly, new claims 33 to 47 depend from independent claims 21 but are otherwise substantially similar to original claims 2 through 17 which depend from independent claim 1. New claim 48 is substantially similar to original claim 18 except that new claim 48 is directed to treatment using a vector comprising a polynucleotide encoding a VEGF-D polypeptide. Polynucleotides encoding a VEGF-D polypeptide are supported in the specification, for example, at page 21, lines 7-27 and in original claim 21. New claims 49-72 are supported by the specification as filed as indicated in attached Appendix C.

II. The Information Disclosure Statement should be considered.

The Examiner indicated that the information disclosure statement filed August 24, 2000 failed to comply with 37 C.F.R. §1.98(a)(2) and 37 C.F.R. §1.98(a)(1), alleging that copies of the documents cited in the PTO Form 1449 were not submitted with the information disclosure statement. The information disclosure statement was not considered. Applicants respectfully traverse the objection, because copies of all the cited documents were timely filed as part of the information disclosure statement. Attached herewith as Appendix D is a copy of a stamped, dated postcard received from the Patent and Trademark Office indicating receipt of the information disclosure statement "...w/25US, 15 FOR, 88OTH..." thereby establishing that Applicants submitted 25 U.S. patents, 15 foreign patent publications and 88 other references. Thus, the information disclosure statement was in full compliance with the requirements of 37 C.F.R. §§1.98(a)(1) and (a)(2), and should have been considered. However, since the documents appear to have been misplaced

at the Patent and Trademark Office, copies of these documents are being re-submitted herewith. Applicants respectfully request that the information disclosure statement filed August 24, 2000 be considered.

III. The Rejection of Claims under 35 U.S.C. §112, first paragraph should be withdrawn.

Claims 1-18 and 21-30 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. (See Office Action at pages 4-11.) Applicants respectfully traverse.

The Examiner rejected claims to a method of "preventing" restenosis and stenosis but indicated that claims to a method of "inhibiting" restenosis or stenosis are enabled by the specification. Apparently, it is the Examiner's position that because gene therapy is a highly unpredictable art and because "prevention" allegedly is synonymous with complete amelioration or cure of restenosis/stenosis, then the claims to methods of preventing restenosis are not enabled by the specification. (Office Action at pages 4-7.) The Examiner acknowledged that:

> **"...The above rejections could be overcome by amending all claims to recite that stenosis or restenosis is inhibited rather than "prevented"..." (Official Action at page 11).**

While Applicants respectfully disagree with the Examiner's position that the term "prevention" means only complete prevention, in order to expedite prosecution and facilitate an early allowance of the claims of the instant application, the Applicants have adopted the Examiner's suggestion. The claims have been amended herein such that the terms "prevent", "preventing" and "prevention" have been replaced with the terms "inhibit", "inhibiting" and "inhibition", respectively. Applicants believe that those of skill in the art will understand that the term "inhibition" encompasses any amount of therapeutically beneficial effect and have always intended to pursue claims of such scope. The Examiner indicated at page 11

of the Official Action that such an amendment would obviate the grounds for the rejection. Applicants therefore request that the rejection be withdrawn.

The Examiner further rejected the claims because claims 1 and 21 did not recite a promoter, alleging that as such the claims encompass administering a gene without a promoter and the specification fails to teach that administering a polynucleotide encoding VEGF-C or VEGF-D without expression would be effective in treating and preventing restenosis. (Office Action at pages 7-8.) The Examiner indicated that the rejection would be overcome by reciting operable linkage to a promoter. (Office Action at page 11.) Applicants have adopted this suggestion and amended claims 1, 21, 22 and 26-29 to recite of a promoter linked to the polynucleotide. Applicants request that the rejection therefore be withdrawn as moot.

As a further basis for rejection the Examiner stated that claims 1-18 and 21 encompassed systemic delivery, and alleged that the specification only enables delivery of the polynucleotide to the location of the target cells to inhibit restenosis or stenosis. (Office Action at pages 8-10.) Applicants traverse the rejection. The specification, in the paragraph bridging pages 9 and 10, specifically contemplates administering using any medically-accepted means for introducing a therapeutic. Those of skill in the art know how to administer therapeutic agents by injection, oral ingestion, intranasal topical or numerous other routes of administration. In light of the fact that these routes of administration are contemplated in the specification, Examiner's position is incongruous with the enablement requirements of 35 U.S.C. §112, first paragraph.

Nevertheless, in an attempt to expedite prosecution, Applicants have amended claims 1 and 21 to recite that the administering is carried out "...locally at the site of said stenosis or restenosis..."[1] Applicants believe this amendment overcomes the rejection and request that the rejection be withdrawn.

Applicants believe the amendments and responses presented above remove the grounds for rejection of the claims based on 35 U.S.C. §112, first

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[1] It will be appreciated that there is continual blood flow through blood vessels, and the recitation that administration is local to the site of treatment is not intended to imply that all of the therapeutic composition must remain at the focus of administration.

paragraph. Applicants request withdrawal of the rejection and reconsideration of the application in light of this response.

IV. Rejection of Claims under 35 U.S.C. §112, second paragraph should be withdrawn.

The Examiner rejected claims 1-17 and 21 under 35 U.S.C. §112, second paragraph for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. It was the Examiner's position that claims 1 and 21 were incomplete because it was unclear how administration without expression correlates to a treatment of a subject to prevent stenosis or restenosis of a blood vessel. To clarify the claims, Applicants have amended claims 1 and 18 to positively recite "...wherein expression of said VEGF-C in said blood vessel inhibits..." and 21 to positively recite "...wherein expression of said VEGF-D in said blood vessel inhibits..." stenosis or restenosis. This amendment overcomes the rejection and places the claims in condition for allowance.

V. Conclusion

Applicants believe all the claims are now in a condition for allowance. Favorable reconsideration of the application is respectfully requested. The Examiner is invited to contact the undersigned with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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